

# Wegener's Granulomatosis

## Overview

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Wegener's granulomatosis is a rare disease, in which the blood vessels and other tissues become inflamed. This inflammation damages important organs of the body by limiting blood flow to those organs and destroying normal tissue.

Although the disease can involve any organ system, Wegener's granulomatosis mainly affects the respiratory tract (sinuses, nose, trachea (windpipe), and lungs) and kidneys. This disorder can affect people at any age and strikes men and women equally. It is rare in African Americans compared to Caucasians. Health experts do not know what causes Wegener's granulomatosis.

## Symptoms

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The first symptoms of Wegener's granulomatosis are often vague and frequently include upper respiratory tract symptoms, joint pains, weakness, and tiredness.

### Upper respiratory tract

The most common sign of Wegener's granulomatosis is involvement of the upper respiratory tract, which occurs in nearly all patients. Symptoms include sinus pain, discolored or bloody fluid from the nose, and nasal ulcers. A common sign of the disease is almost constant rhinorrhea ("runny nose") or other cold symptoms that do not respond to usual treatment or that become increasingly worse. It is noteworthy that other more common diseases (such as allergies) can produce constant rhinorrhea, and Wegener's granulomatosis is a rare cause of this symptom.

Rhinorrhea in Wegener's granulomatosis results from nasal inflammation or sinus drainage and can cause pain. A hole may develop in the cartilage of the nose, which may lead to collapse (called saddle-nose deformity). The eustachian tubes, which are important for normal ear function, may become blocked, causing chronic ear problems and hearing loss. Bacterial infection can complicate Wegener's-related sinusitis (inflammation of the sinuses) with congestion and chronic sinus pain.

### Lungs

The lungs are affected in most people with Wegener's granulomatosis, although no symptoms may be present. If symptoms are present, they include cough, hemoptysis (coughing up blood), shortness of breath, and chest discomfort.



## Kidneys

Kidney involvement, which occurs in more than three-fourths of people with this disorder, usually does not cause symptoms. If detected by blood and urine tests, a doctor can start proper treatment, preventing long-term damage to the kidneys.

## Musculoskeletal system

Pain in the muscles and joints or, occasionally, joint swelling affects two-thirds of people with Wegener's granulomatosis. Although joint pain can be very uncomfortable, it does not lead to permanent joint damage or deformities.

## Eyes

Wegener's granulomatosis can affect the eyes in several ways. People may develop

- Conjunctivitis (inflammation of the conjunctiva, the inner lining of the eyelid)
- Scleritis (inflammation of the scleral layer, the white part of the eyeball)
- Episcleritis (inflammation of the episcleral layer, the outer surface of the sclera)
- Mass lesion behind the eye globe

Symptoms in the eye include redness, burning, or pain. Double vision or a decrease in vision are serious symptoms requiring immediate medical attention.

## Skin lesions

Nearly half of people with Wegener's granulomatosis develop skin lesions. These often have the appearance of small red or purple raised areas or blister-like lesions, ulcers, or nodules that may or may not be painful.

## Other symptoms

Some people experience narrowing of the trachea. The symptoms can include voice change, hoarseness, shortness of breath, or cough.

The nervous system and heart occasionally may be affected. Fever and night sweats may occur. Fever also may signal an infection, often of the upper respiratory tract.

## Diagnosis

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To treat people with Wegener's granulomatosis most effectively, healthcare professionals must diagnose the disease early. There are no blood tests that a doctor can use to diagnose Wegener's granulomatosis, but blood tests are important to rule out other causes of illness and to determine which organ may be affected.

Most blood tests can only suggest that a person has inflammation somewhere in the body. Anemia (low red blood cell count), elevated white blood cell count and platelet count, and an elevated sedimentation rate are commonly found in people with Wegener's granulomatosis. If the kidneys are

involved, a healthcare professional can see red blood cells and structures called red blood cell casts in the urine when viewed under a microscope, and the blood tests measuring kidney function may show abnormalities.

X-ray results can be very helpful in diagnosing Wegener's granulomatosis. People with lung problems will have abnormal chest X-rays. CT (computed tomography) scans in people with sinus problems may show thickening of the sinus lining.

Many people with active Wegener's granulomatosis have a blood test that shows the presence of a specific type of antibody (a disease-fighting protein) called antineutrophil cytoplasmic antibodies (ANCA). Although a positive ANCA test is useful to support a suspected diagnosis of Wegener's granulomatosis, in most instances healthcare professionals do not use it by itself to diagnose this disorder. The ANCA test may be negative in some people with active Wegener's granulomatosis.

Currently, the only clear-cut way to diagnose Wegener's granulomatosis is by performing a biopsy (removing a tiny piece of tissue) of an involved organ (usually the sinuses, lung, or kidney). A healthcare professional will examine tissue from the organ under the microscope to confirm the presence of vasculitis and granulomas (a specific type of inflammation), which together are features of Wegener's granulomatosis. A biopsy is very important both to confirm the presence of the disease and also to make sure other disorders that may have similar signs and symptoms are not present.

## Treatment

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With the appropriate treatment, the outlook is good for people with Wegener's granulomatosis. In a study of 158 patients who were treated with prednisone and cyclophosphamide at the National Institutes of Health (NIH), 91 percent markedly improved. After 6 months to 24 years of follow-up, 80 percent survived.

In most cases, treatment consists of a combination of a glucocorticoid (a steroid) and a cytotoxic medicine. Although these medicines are helpful in treating Wegener's granulomatosis, people and their healthcare professionals should be aware that they potentially have serious side effects. Often, by working together, they can minimize side effects by carefully monitoring the treatment.

Approximately half of people with Wegener's granulomatosis may experience a return of their disease. This occurs most frequently within 2 years of stopping medicine but can occur at any point both during treatment or after stopping treatment. Thus, it is extremely important that people continue to see their healthcare professionals regularly, both while they are on these medicines, as well as after the medicines have been stopped.

### Prednisone

Prednisone is the most common glucocorticoid that healthcare professionals use. Prednisone is similar to cortisol, the natural glucocorticoid hormone produced by the body. It is chemically different from the anabolic steroids that have been used by athletes and is given in doses much higher than the body normally produces. Healthcare professionals usually give prednisone as a single morning dose to try to imitate how the body normally secretes cortisol.

When the person's illness improves, the prednisone dose is gradually decreased and converted to an every-other-day dosing schedule, usually over a period of 3 to 4 months. With further improvement in the disease, prednisone is gradually decreased and discontinued completely after approximately 6 to 12 months.

When prednisone is taken by mouth, the body stops making its own natural cortisol. As the prednisone dose is gradually reduced, the body will resume making cortisol again. It is extremely important that prednisone never be stopped suddenly because the body requires prednisone (or cortisol) to function and may not be able to immediately make what it needs.

Prednisone can affect the body's ability to fight off infection. People taking this medicine should report immediately any symptoms of infection and, specifically, any fever to their healthcare professionals. Prednisone can also cause weight gain, cataracts, brittle bones, diabetes, and changes in mood and personality.

## **Cyclophosphamide**

Cyclophosphamide (Cytoxan) is the cytotoxic drug most commonly used to treat Wegener's granulomatosis. People take cyclophosphamide once a day by mouth and must take the drug all at once in the morning followed by drinking a large amount of liquid. Although the first dose of cyclophosphamide is based on the person's weight and kidney function, the healthcare professional may adjust the dosage based on blood counts, which are monitored closely to be sure that the white blood cell count is maintained at a safe level.

In the original regimen, cyclophosphamide was continued for a full year beyond that point at which the disease was in remission. The dose of cyclophosphamide was then decreased gradually and eventually stopped. In more recent treatment approaches, however, cyclophosphamide is either not used at all or given only to patients with severe disease manifestations. When cyclophosphamide is used, it is only administered until remission is achieved and then switched to another, less toxic medication such as methotrexate or azathioprine (discussed below).

Cyclophosphamide is a powerful medicine that keeps the immune system from working normally. The doctor must monitor their patients carefully and perform blood tests frequently. Cyclophosphamide can cause an increased risk of infection, bone marrow suppression (lowering of blood counts), sterility, hemorrhagic cystitis (bleeding from the bladder), bladder cancer, as well as other serious side effects.

## **Methotrexate**

Methotrexate has been studied at NIH for treating Wegener's granulomatosis since 1990. In people with active, but not immediately threatening, Wegener's granulomatosis, methotrexate has been used in combination with prednisone to bring about remission. It also is used to maintain remission after a person has initially received cyclophosphamide. Methotrexate is usually given for 1 to 2 years, and if people stay in remission, it is decreased and stopped.

Methotrexate is given once a week usually by mouth, but occasionally as an injection under the skin or in the muscle. People taking methotrexate need to have regular blood work to monitor their response and to watch for side effects.

The side effects of methotrexate include infection, lowering of the blood counts, nausea, soreness and ulceration of the mouth lining, irritation of the lungs (pneumonitis), and inflammation and scarring of the liver. People taking methotrexate cannot drink alcoholic beverages. Methotrexate cannot be given to people who have poor kidney function or who have underlying liver disease such as hepatitis.

## Azathioprine

Azathioprine (also called Imuran) is used primarily to maintain remission in people who have initially been treated and gone into remission with cyclophosphamide. It is taken once a day by mouth. Similar to methotrexate, it is usually given for 1 to 2 years after which time the dosage is lowered until it is stopped.

The side effects of azathioprine include infection, lowering of the blood counts, and, rarely, an allergic type reaction. In people who receive azathioprine to prevent rejection of a transplanted organ, there has been a suggestion of an increased risk of blood cancers (leukemia and lymphoma), but whether this risk exists in other situations is unclear. People with poor kidney function or liver disease can take azathioprine.

## Rituximab

Rituximab (Rituxan) is an antibody that selectively reduces specific types of immune cells (B cells) circulating in the blood. It currently is used to treat certain types of lymphoma and rheumatoid arthritis. Recent studies of rituximab suggest this medicine, when given along with prednisone, effectively induces remission in select patients who have Wegener's granulomatosis. In April 2011, the Food and Drug Administration approved rituximab, in combination with glucocorticoids, for treating Wegener's granulomatosis. Researchers are still studying the long-term effects of rituximab on maintaining remission.

## Other medicines

During the course of treating Wegener's granulomatosis, healthcare professionals often give their patients other medicines to prevent medicine-related side effects. These include:

- Trimethoprim/sulfamethoxazole (also called bactrim or septr), given three times a week to prevent *Pneumocystis carinii* infection (a lung infection)
- A medicine regimen, often given to prevent prednisone-related bone loss (osteoporosis)
- Folic acid or folinic acid (also called leucovorin), often given to people taking methotrexate

## Research

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Since the 1970s, research physicians at the National Institute of Allergy and Infectious Diseases (NIAID), a part of NIH, have been interested in Wegener's granulomatosis. NIAID scientists first introduced the combination of glucocorticoids with cyclophosphamide for treating people with this disease. While this was a dramatic breakthrough for the treatment of Wegener's granulomatosis, researchers realize that these medicines have serious side effects and cannot be tolerated by all people.

Therefore, NIH researchers have continued to study Wegener's granulomatosis to understand the causes of the disease and to develop new treatments.

NIAID and other parts of NIH support research on Wegener's granulomatosis and related forms of vasculitis at medical centers throughout the country through the extramural grants program. NIH helps support the Vasculitis Clinical Research Consortium (VCRC), for example. The multi-center VCRC fosters and facilitates clinical investigation in the inflammatory vasculitides, including Wegener's granulomatosis.

VCRC has four major U.S. vasculitis centers:

- Boston University School of Medicine, Massachusetts
- The Cleveland Clinic, Ohio
- The Johns Hopkins Vasculitis Center, Baltimore, Maryland
- The Mayo Clinic College of Medicine, Rochester, Minnesota

## More Information

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### National Library of Medicine

#### MedlinePlus

8600 Rockville Pike

Bethesda, MD 20894

888-FIND-NLM (888-346-3656) or 301-594-5983

[www.medlineplus.gov](http://www.medlineplus.gov)

### American Autoimmune Diseases Related Association

22100 Gratiot Avenue

East Detroit, MI 48021

586-776-3900

[www.aarda.org](http://www.aarda.org)

### Vasculitis Foundation

P.O. Box 28660

Kansas City, MO 64188-8660

800-277-9474 or 816-436-8211

[www.vasculitisfoundation.org](http://www.vasculitisfoundation.org)



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